Access DB# 77666

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Paul Prebilic Examiner # : 65450 Date: 10/10/02
Art Unit: 3738 Phone Number 308-2905 Serial Number: 9/186,810
Mail Box and Bldg/Room Location: CP2-2D27 Results Format Preferred (circle): (PAPER) DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc., if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Medical Devices With Associated Growth Factors
Inventors (please provide full names): Wenda C. Carlyle, Sheila J. Kelly, Matthew F. Ogle

Earliest Priority Filing Date: Jan. 27, 1998

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

double check for genetic sequence in spec. If so, needs to comply w/ sequence rules (Contact 308-4212 for help desk Mark Spencer.

search the follow databases

- CAPlus
- Medline
- Biosis
- Embase
- Scisearch
- Aidsline

and search subject matter of claims 28-35 (attached). Note claim 34 which is more comprehensive than claim 28.

(10:53 AM)

OCT 10 2002

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STAFF USE ONLY		Type of Search		Vendors and cost where applicable	
Searcher:	JEANNE HORRIGAN	NA Sequence (#)		STN	✓ $147.93
Searcher Phone #:	305-6934	AA Sequence (#)		Dialog	✓ $68.28
Searcher Location:	CP2-2C08	Structure (#)		Questel/Orbit	
Date Searcher Picked Up:	10/10	Bibliographic	✓	Dr.Link	
Date Completed:	10/15	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	196	Fulltext	✓	Sequence Systems	
Clerical Prep Time:		Patent Family		WWW/Internet	
Online Time:	34	Other		Other (specify)	

PTO-1590 (8-01)

2:15

Documentation for 77359
October 10, 2002

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     (FILE 'HOME' ENTERED AT 14:36:14 ON 10 OCT 2002)
     FILE 'REGISTRY' ENTERED AT 14:36:22 ON 10 OCT 2002
                E TAT PROTEIN/CN
L1            7 S E4-E10
                E TAT PROTEIN (BOVINE/CN
                E TAT PROTEIN (HUMAN/CN
L2            9 S E4-E12
L3          212 S TAT PROTEIN?/CN
                E POLYPEPTIDE GROWTH FACTOR/CN
                E VEGF/CN
L4           51 S VEGF?/CN
                E VASCULAR ENDOTHELIAL GROWTH FACTOR/CN
L5            1 S E3
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     10 OCT 2002
L6        18614 S L3 OR L4 OR L5
L7      1283827 S SUBSTRATE
L8      1467672 S ARTIFICIAL OR SYNTHETIC
L9          267 S BIOCOMPATIBLE AND BIORESORBABLE
L10      271293 S CROSSLINK?
L11         112 S L6 AND L7
L12           5 S L10 AND L11
L13          10 S L11 AND L8
L14           0 S L11 AND L9
L15           2 S L12 AND L13
L16          13 S L12 OR L13
L17          11 S L16 NOT L15
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              39.41     118.66
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                              -1.86      -1.86
STN INTERNATIONAL LOGOFF AT 14:46:56 ON 10 OCT 2002


File 350:Derwent WPIX 1963-2002/UD,UM &UP=200264
File 344:Chinese Patents Abs Aug 1985-2002/Sep
File 347:JAPIO Oct 1976-2002/Jun(Updated 021004)
File 371:French Patents 1961-2002/BOPI 200209
Set     Items   Description
S1          4   AU='CARLYLE W C'
S2         25   AU='KELLY S J'
S3         13   AU='OGLE M F'
S4          1   S1 AND S2 AND S3
S5         38   S1:S3 NOT S4
S6        125   TAT()PROTEIN
S7          1   S5 AND S6

File 348:EUROPEAN PATENTS 1978-2002/Sep W05
File 349:PCT FULLTEXT 1983-2002/UB=20021003,UT=20020926
Set     Items   Description
S1          9   AU='CARLYLE WENDA':AU='CARLYLE WENDA C'
S2          4   AU='KELLY SHEILA J'
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S3          28   AU='OGLE MATTHEW F'
S4           2   S1 AND S2 AND S3
S5           2   PN='WO 9937337'
S6           1   PN='EP 1051204'
S7           2   PN='WO 200141825'
S8           0   S4 NOT S5:S7
S9          31   S1:S3 NOT S5:S7
S10        880   TAT()PROTEIN
S11          0   S9 AND S10

File 155:MEDLINE(R) 1966-2002/Sep W5
File   5:Biosis Previews(R) 1969-2002/Oct W1
File  73:EMBASE 1974-2002/Oct W1
File  34:SciSearch(R) Cited Ref Sci 1990-2002/Oct W2
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
Set     Items   Description
S1         28   AU='CARLYLE W':AU='CARLYLE W C'
S2         12   AU='CARLYLE W.':AU='CARLYLE W.C.'
S3         27   AU='CARLYLE WC':AU='CARLYLE WENDA C'
S4        178   AU='KELLY S J'
S5          4   AU='KELLY S.K.'
S6        106   AU='KELLY SJ'
S7         70   AU='KELLY S.J.'
S8          1   AU='OGLE M F'
S9          1   AU='OGLE M.F.'
S10        15   AU='OGLE MATTHEW':AU='OGLE MATTHEW FRANK'
S11         1   AU='OGLE MF'
S12         1   S1:S3 AND (S4 OR S6 OR S7) AND S8:S11
S13        28   S1
S14       435   (S1:S4 OR S6:S11) NOT S12
S15      6468   TAT()PROTEIN
S16         0   S14 AND S15



File 155:MEDLINE(R) 1966-2002/Sep W5
Set     Items   Description
S1        876   TAT()PROTEIN
S2     182342   SUBSTRATE?
S3         37   S1 AND S2
S4         16   S3/2002 OR S3/2001 OR S3/2000 OR S3/1999
S5         21   S3 NOT S4
S6          0   POLYPEPTIDE()GROWTH()FACTOR? ? AND TAT()PROTEIN? ? AND (VE-
               GF OR VASCULAR()ENDOTHELIAL()GROWTH()FACTOR? ?)
S7        919   TAT()PROTEIN? ?
S8     182331   SUBSTRATE? ?
S9      17901   BIOCOMPATIBLE
S10       302   BIORESORBABLE
S11    238476   ARTIFICIAL OR SYNTHETIC
S12    812627   TISSUE OR ORGAN
S13    225247   PROSTHES?S OR GRAFT? ?
S14        41   S7 AND S8
S15   1206826   S11:S13
S16         6   S14 AND S9:S13
10oct02 14:34:32 User262807 Session D3773.6
$10.88  Estimated total session cost   2.702 DialUnits
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$57.40 Estimated total session cost 6.659 DialUnits
Status: Signed Off. (10 minutes)

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     (FILE 'HOME' ENTERED AT 11:11:58 ON 15 OCT 2002)
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L1          212 S TAT PROTEIN?/CN
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     15 OCT 2002
L2           90 S L1
L3        11231 S TAT(L)PROTEIN#/OBI
                E "PROSTHETIC MATERIALS AND PROSTHETICS"/CT
                E E3
L4        22867 S E3
                E MEDICAL GOODS/CT
L5        19980 S E3
L6            1 S (L2 OR L3) AND (L4 OR L5)
L7         5661 TAT(W) PROTEIN?
L8        11603 L2 OR L3 OR L7
L9            1 L8 AND (L4 OR L5)
L10           0 L9 NOT L6
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	24.68	29.27

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.62	-0.62

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 SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 11:18:19 ON 15 OCT 2002
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=> d scan

L103 1 ANSWERS CAPLUS COPYRIGHT 2002 ACS
IC ICM A61L027-00
CC 63-7 (Pharmaceuticals)
TI Prostheses with associated growth factors
ST prosthesis polypeptide growth factor; vascular endothelial growth factor prosthesis
IT Ring
(annuloplasty; prostheses with assocd. growth factors)
IT Artery
Blood vessel
(artificial; prostheses with assocd. growth factors)
IT Animal tissue
(bovine peripheral; prostheses with assocd. growth factors)
IT Blood vessel
(endothelium; prostheses with assocd. growth factors)
IT Glues
(fibrin; prostheses with assocd. growth factors)
IT Medical goods
(pledgets or patches; prostheses with assocd. growth factors)
IT Electric contacts
Prosthetic materials and Prosthetics
(prostheses with assocd. growth factors)
IT Transplant and Transplantation
Transplant and Transplantation
(skin; prostheses with assocd. growth factors)
IT Medical goods
(stents; prostheses with assocd. growth factors)
IT Medical goods
(sutures; prostheses with assocd. growth factors)
IT Canidae
Cattle
Kangaroo
(tissues; prostheses with assocd. growth factors)
IT Skin
Skin
(transplant; prostheses with assocd. growth factors)
IT Heart
(valve, porcine; prostheses with assocd. growth factors)
IT Peptides, biological studies
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular endothelial growth factor; prostheses with assocd. growth factors)
IT 127464-60-2, Vascular endothelial growth factor
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prostheses with assocd. growth factors)
IT 111-30-8, Glutaraldehyde
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vascular endothelial growth factor; prostheses with assocd. growth factors)

ALL ANSWERS HAVE BEEN SCANNED

L6 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:429539 HCAPLUS
DOCUMENT NUMBER: 137:24286
TITLE: Chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition
INVENTOR(S): Gyuris, Jeno; Lamphere, Lou; Beach, David H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. 5,672,508.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002068706	A1	20020606	US 1997-902572	19970729
US 5672508	A	19970930	US 1996-589981	19960123
CA 2242960	AA	19970731	CA 1997-2242960	19970117
WO 9906540	A2	19990211	WO 1998-US15759	19980729
WO 9906540	A3	19991216		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886014	A1	19990222	AU 1998-86014	19980729
EP 1000166	A2	20000517	EP 1998-937264	19980729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001512008	T2	20010821	JP 2000-505282	19980729

PRIORITY APPLN. INFO.: US 1996-589981 A2 19960123
US 1997-902572 A2 19970729
WO 1998-US15759 W 19980729

AB The present invention pertains to novel inhibitors of cyclin-dependent kinases (CDKs), particularly CDK/cyclin complexes, which inhibitors can be used to control proliferation and/or differentiation of cells in which the inhibitors are introduced. The invention provides six novel fusion proteins of protein p27 and p16.

these are the index terms for the abstract above.

L6 1 ANSWERS HCAPLUS COPYRIGHT 2002 ACS
IC ICM A61K031-70
ICS C12N015-63; C07H021-04
NCL 514044000
CC 63-3 (Pharmaceuticals)
Section cross-reference(s): 1, 3, 6
TI Chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition
ST chimeric protein p16 p27 cyclin dependent kinase inhibitor sequence; cell cycle progression inhibition chimeric protein p16 p27 CDK
IT Ankyrins

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(-like, CDK-binding motif contg.; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Bcl-x; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(DOT; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Transcription factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(I.kappa.B (inhibitor of NF-.kappa.B); chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Transcription factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Rb; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antepennepedia; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bcl-2; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Biological transport
(calcium mobilization, ion permeability; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Drug delivery systems
(carriers; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT ***Medical goods***
(catheters, for recombinant transfection; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Cell death
Cell differentiation
Gene therapy
Genetic vectors
Phosphorylation, biological

Protein engineering
Retroviral vectors
Transformation, genetic
Virus vectors
Wound healing
(chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Clathrin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Platelet-derived growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Transcription factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT p53 (protein)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(diphtheria; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Cell proliferation
(endothelial, stimulating; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Toxins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(exotoxin A, Pseudomonas; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Gene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(expression; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Cyclin dependent kinase inhibitors
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(fusion proteins; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT RGD peptides
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL

(Biological study); PREP (Preparation); USES (Uses)
(fusion proteins; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Molecular association
(inhibition of; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Blood vessel, disease
(injury, treatment of; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Endothelium
(integrity, breech of; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Biological transport
(internalization, peptide; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Drug delivery systems
(liposomes; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Nucleosides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metab. of; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Angiogenesis
(neovascularization; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Fusion proteins (chimeric proteins)
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(of p16/p27; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(p15; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Cyclin dependent kinase inhibitors
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(p16INK4A; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(p18; chimeric protein of human protein p27 and p16 as cyclin-dependent

kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(p19; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Protein motifs
(p21/p27 inhibitory domain; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(p21CIP1/WAF1; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(p27; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Cyclin dependent kinase inhibitors
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(p27KIP1; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Cyclin dependent kinase inhibitors
(p57KIP2; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Chelating agents
(pharmaceutical, protein; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT mRNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polycistronic; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Signal transduction, biological
(protein for; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Stability
(protein; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Artery, disease
(restenosis, treatment of; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Muscle

(smooth, proliferation; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Cell migration
(stimulating; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(***tat*** , HIV; chimeric ***protein*** of human ***protein*** p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tubby; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor-inhibiting; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Adeno-associated virus
Adenoviridae
Human herpesvirus
(vectors; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Transforming growth factors
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.beta.-; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT Hemolysins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.delta.-hemolysins; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 433988-77-3P 433988-80-8P 433988-81-9P 433988-82-0P 433988-83-1P
433988-84-2P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 433988-85-3, Protein p27 (human fragment) 433988-86-4
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(amino acid sequence; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 37231-28-0, Melittin 67995-63-5, Pardaxin 72093-21-1, Mastoparan, 80295-59-6, Complement C9 131257-09-5, Bombolitin 150428-23-2, Cyclin-dependent kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 106096-92-8, Acidic fibroblast growth factor 106096-93-9, Basic fibroblast growth factor 127464-60-2, Vascular endothelial growth factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 15421-51-9, Inositol phosphate
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metab. of; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 433988-71-7P 433988-72-8P 433988-73-9P 433988-74-0P 433988-75-1P 433988-76-2P 433988-78-4P 433988-79-5P 433988-89-7P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 433988-87-5
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 433989-60-7 433989-62-9 433989-63-0 433989-65-2 433989-67-4
RL: PRP (Properties)
(unclaimed nucleotide sequence; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 433989-61-8 433989-64-1 433989-66-3 433989-68-5
RL: PRP (Properties)
(unclaimed protein sequence; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

IT 96573-46-5 99616-33-8 103233-04-1 131399-94-5 255039-62-4 272127-79-4 433989-69-6
RL: PRP (Properties)
(unclaimed sequence; chimeric protein of human protein p27 and p16 as cyclin-dependent kinase inhibitor and uses thereof for cell-cycle progression inhibition)

(FILE 'HOME' ENTERED AT 11:11:58 ON 15 OCT 2002)
FILE 'REGISTRY' ENTERED AT 11:12:14 ON 15 OCT 2002
L1 212 S TAT PROTEIN?/CN
FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 11:12:35 ON 15 OCT 2002
L2 90 S L1
L3 11231 S TAT(L)PROTEIN#/OBI
E "PROSTHETIC MATERIALS AND PROSTHETICS"/CT
E E3
L4 22867 S E3
E MEDICAL GOODS/CT

```
L5         19980 S E3
L6             1 S (L2 OR L3) AND (L4 OR L5)
L7          5661 TAT(W) PROTEIN?
L8         11603 L2 OR L3 OR L7
L9             1 L8 AND (L4 OR L5)
L10            0 L9 NOT L6
```

into a patient for extended periods of time.
ADVANTAGE - The invention has components that have been modified with a compound that stimulates cell adhesion.
pp; 63 DwgNo 0/16
Derwent Class: D16; D22; L02; P34
International Patent Class (Main): A61L-027/22
International Patent Class (Additional): A61L-027/10; A61L-027/30; A61L-027/50; A61L-029/04; A61L-031/04

File 350:Derwent WPIX 1963-2002/UD,UM &UP=200264
File 344:Chinese Patents Abs Aug 1985-2002/Sep
File 347:JAPIO Oct 1976-2002/Jun(Updated 021004)
File 371:French Patents 1961-2002/BOPI 200209

Set	Items	Description
S1	4	AU='CARLYLE W C'
S2	25	AU='KELLY S J'
S3	13	AU='OGLE M F'
S4	**1**	**S1 AND S2 AND S3**
S5	38	S1:S3 NOT S4
S6	125	TAT()PROTEIN
S7	**1**	**S5 AND S6**

File 348:EUROPEAN PATENTS 1978-2002/Sep W05
File 349:PCT FULLTEXT 1983-2002/UB=20021003,UT=20020926

Set	Items	Description
S1	9	AU='CARLYLE WENDA':AU='CARLYLE WENDA C'
S2	4	AU='KELLY SHEILA J'
S3	28	AU='OGLE MATTHEW F'
S4	2	S1 AND S2 AND S3
S5	2	PN='WO 9937337'
S6	1	PN='EP 1051204'
S7	2	PN='WO 200141825'
S8	0	S4 NOT S5:S7
S9	31	S1:S3 NOT S5:S7
S10	880	TAT()PROTEIN
S11	0	S9 AND S10

2027

OCT 15 2002

Paul Prebilic
AU 3738

12/7/1 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.
07225916 Genuine Article#: 131UV Number of References: 0
Title: Accelerated endothelialization of bioprosthetic heart valve leaflets with vascular endothelial growth factor
Author(s): Carlyle WC ; Kelly SJ ; Ogle MF ; Mirsch W
Corporate Source: ST JUDE MED INC,/ST PAUL//MN/
Journal: CIRCULATION, 1998, V98, N17,S (OCT 27), P1708-1708
ISSN: 0009-7322 Publication date: 19981027
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436
Language: English Document Type: MEETING ABSTRACT

File 155:MEDLINE(R) 1966-2002/Sep W5
File 5:Biosis Previews(R) 1969-2002/Oct W1
File 73:EMBASE 1974-2002/Oct W1
File 34:SciSearch(R) Cited Ref Sci 1990-2002/Oct W2

4/7/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX

012672885
WPI Acc No: 1999-478992/199940
Prosthesis carrying polypeptide growth factor to stimulate attachment of viable cells, particularly allografts or xenografts, e.g. porcine heart valves, - has better durability with reduced calcification and inflammation.
Patent Assignee: ST JUDE MEDICAL INC (SJUD-N)
Inventor: CARLYLE W C ; KELLY S J ; OGLE M F
Number of Countries: 082 Number of Patents: 006
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9937337	A2	19990729	WO 99US1391	A	19990121	199940 B
AU 9924658	A	19990809	AU 9924658	A	19990121	200001
EP 1051204	A2	20001115	EP 99904210	A	19990121	200059
			WO 99US1391	A	19990121	
CN 1289259	A	20010328	CN 99802428	A	19990121	200140
BR 9907273	A	20010904	BR 997273	A	19990121	200160
			WO 99US1391	A	19990121	
JP 2002500929	W	20020115	WO 99US1391	A	19990121	200207
			JP 2000528316	A	19990121	

Priority Applications (No Type Date): US 98186810 A 19981105; US 9814087 A 19980127
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9937337	A2	E	54	A61L-027/00	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9924658	A		A61L-027/00	Based on patent WO 9937337
EP 1051204	A2	E	A61L-027/00	Based on patent WO 9937337

Designated States (Regional): CH DE ES FR GB IE IT LI NL

CN 1289259	A		A61L-027/00	
BR 9907273	A		A61L-027/00	Based on patent WO 9937337
JP 2002500929	W	52	A61F-002/02	Based on patent WO 9937337

Abstract (Basic): WO 9937337 A2

NOVELTY - Prosthesis (A) comprises a substrate (S) and an associated polypeptide growth factor (I) that stimulates association of viable cells with (S).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) method of associating endothelial cells (EC) with a substrate by treating (A) with a culture of EC;

(b) production of a biocompatible material (B) by adhering (I) to a substrate;

(c) an article comprising crosslinked tissue with associated VEGF (vascular endothelial growth factor); and

(d) prosthetic heart valve associated with VEGF.

ACTIVITY - None given.

MECHANISM OF ACTION - MECHANISM OF ACTIVITY - (I) stimulates chemotaxis and proliferation of endothelial cells.

USE - (A) are used for repair/replacement of damaged tissues or organs, in particular it is a porcine heart valve prosthesis. Other biomedical devices, e.g. catheters, can be treated similarly with (I).

ADVANTAGE - Attachment of (I) stimulates attachment of (endothelial) cells, so improves the performance of the prosthesis, particularly its long-term durability (by reducing calcification), and also reduces the risk of infection and inflammation. Also attachment of endothelial cells promotes further recruitment of other cells able to repair/remodel the tissue. With crosslinked tissue, (I) also reduces cellular toxicity resulting from treatment with glutaraldehyde.

pp; 54 DwgNo 0/8

Derwent Class: B04; D16; D22; P32; P34
International Patent Class (Main): A61F-002/02; A61L-027/00
International Patent Class (Additional): A61F-002/04; A61F-002/10; A61F-002/24; A61K-038/22; A61K-047/48; A61L-031/00

7/7/1 (Item 1 from file: 350)
DIALOG(R)File 350:Derwent WPIX
(c) 2002 Thomson Derwent. All rts. reserv.
013897291
WPI Acc No: 2001-381504/200140
Medical article, e.g. heart valve prosthesis, for contacting patient's bodily fluids includes biocompatible material comprising ceramic material, and cell adhesion stimulating protein(s) associated with biocompatible material
Patent Assignee: ST JUDE MEDICAL INC (SJUD-N)
Inventor: BRENDZEL A M; CARLYLE W C
Number of Countries: 023 Number of Patents: 001
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200141825	A1	20010614	WO 2000US33175	A	20001207	200140	B

Priority Applications (No Type Date): US 99459451 A 19991213
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200141825	A1	E	63	A61L-027/22	

Designated States (National): BR CA CN JP
Designated States (Regional): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR

Abstract (Basic): WO 200141825 A1

NOVELTY - A medical article comprises a biocompatible material comprising a ceramic material, and cell adhesion stimulating protein(s) associated with the biocompatible material.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method for producing a medical article as above comprising adhering a cell adhesion stimulating protein to a ceramic material; and

(2) a method for producing a prosthesis comprising:

(a) harvesting viable cells from a patient;

(b) adhering a cell adhesion stimulating protein to a ceramic material; and

(c) associating the viable cells with the ceramic material by contacting the ceramic material having adhered protein with a cell structure comprising the viable cells.

USE - As a medical article, e.g. an artificial organ, a heart valve prosthesis, an annuloplasty ring, a stent, a pledget, suture, an electrical lead, a permanently in-dwelling percutaneous device, an AV shunt, a vascular graft, a dermal graft, or a surgical patch (claimed), useful for contacting a patient's bodily fluids and for implantation

into a patient for extended periods of time.
ADVANTAGE - The invention has components that have been modified with a compound that stimulates cell adhesion.
pp; 63 DwgNo 0/16
Derwent Class: D16; D22; L02; P34
International Patent Class (Main): A61L-027/22
International Patent Class (Additional): A61L-027/10; A61L-027/30; A61L-027/50; A61L-029/04; A61L-031/04

File 350:Derwent WPIX 1963-2002/UD,UM &UP=200264
File 344:Chinese Patents Abs Aug 1985-2002/Sep
File 347:JAPIO Oct 1976-2002/Jun(Updated 021004)
File 371:French Patents 1961-2002/BOPI 200209

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S3	13	AU='OGLE M F'
S4	**1**	**S1 AND S2 AND S3**
S5	38	S1:S3 NOT S4
S6	125	TAT()PROTEIN
S7	**1**	**S5 AND S6**

File 348:EUROPEAN PATENTS 1978-2002/Sep W05
File 349:PCT FULLTEXT 1983-2002/UB=20021003,UT=20020926

Set	Items	Description
S1	9	AU='CARLYLE WENDA':AU='CARLYLE WENDA C'
S2	4	AU='KELLY SHEILA J'
S3	28	AU='OGLE MATTHEW F'
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S5	2	PN='WO 9937337'
S6	1	PN='EP 1051204'
S7	2	PN='WO 200141825'
S8	0	S4 NOT S5:S7
S9	31	S1:S3 NOT S5:S7
S10	880	TAT()PROTEIN
S11	0	S9 AND S10

12/7/1 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci
(c) 2002 Inst for Sci Info. All rts. reserv.
07225916 Genuine Article#: 131UV Number of References: 0
Title: Accelerated endothelialization of bioprosthetic heart valve leaflets with vascular endothelial growth factor
Author(s): Carlyle WC ; Kelly SJ ; Ogle MF ; Mirsch W
Corporate Source: ST JUDE MED INC,/ST PAUL//MN/
Journal: CIRCULATION, 1998, V98, N17,S (OCT 27), P1708-1708
ISSN: 0009-7322 Publication date: 19981027
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436
Language: English Document Type: MEETING ABSTRACT

File 155:MEDLINE(R) 1966-2002/Sep W5
File 5:Biosis Previews(R) 1969-2002/Oct W1
File 73:EMBASE 1974-2002/Oct W1
File 34:SciSearch(R) Cited Ref Sci 1990-2002/Oct W2

File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

Set	Items	Description
S1	28	AU='CARLYLE W':AU='CARLYLE W C'
S2	12	AU='CARLYLE W.':AU='CARLYLE W.C.'
S3	27	AU='CARLYLE WC':AU='CARLYLE WENDA C'
S4	178	AU='KELLY S J'
S5	4	AU='KELLY S.K.'
S6	106	AU='KELLY SJ'
S7	70	AU='KELLY S.J.'
S8	1	AU='OGLE M F'
S9	1	AU='OGLE M.F.'
S10	15	AU='OGLE MATTHEW':AU='OGLE MATTHEW FRANK'
S11	1	AU='OGLE MF'
S12	**1**	**S1:S3 AND (S4 OR S6 OR S7) AND S8:S11**
S13	28	S1
S14	435	(S1:S4 OR S6:S11) NOT S12
S15	6468	TAT()PROTEIN
S16	0	S14 AND S15

5/6,K/1
DIALOG(R)File 155:
09985136 98410624 PMID: 9735304
RNA binding and modulation of PKR activity.
Jul 1998
... Activated PKR phosphorylates eIF2, an essential initiation factor of protein synthesis, as well as other substrates including histone IIA, a 90-kDa protein from rabbit reticulocytes, the inhibitor, IkappaB, of the transcription factor, NF-kappaB, and the HIV-1 Tat protein . PKR interacts with several cellular and viral products and these interactions modulate its activation by...

5/6,K/2
DIALOG(R)File 155:
09936096 98372111 PMID: 9708406
HIV-1 Tat induces tyrosine phosphorylation of p125FAK and its association with phosphoinositide 3-kinase in PC12 cells.
Jul 30 1998
... PC12 cells, either treated with low concentrations (0.1-1 nM) of extracellular HIV-1 Tat protein or stably transfected with Tat cDNA. RESULTS: Extracellular Tat induced a rapid increase of p125FAK...
...PI 3-K but did not affect the total amount of p125FAK. CONCLUSION: HIV-1 Tat protein enhanced both the expression and the functionality of p125FAK in PC12 neuronal cells. Whereas...
Enzyme No.: EC 2.7.1.- (endogenous substrate pp120); EC 2.7.1.112 (Protein-Tyrosine Kinase); EC 2.7.1.137 (1...
Chemical Name: Cell Adhesion Molecules; Gene Products, tat; Tyrosine; endogenous substrate pp120; Protein-Tyrosine Kinase; 1-Phosphatidylinositol 3-Kinase

5/6,K/3
DIALOG(R)File 155:
09711761 98150851 PMID: 9491887
A novel CDK9-associated C-type cyclin interacts directly with HIV-1 Tat and mediates its high-affinity, loop-specific binding to TAR RNA.
Feb 20 1998

The HIV-1 Tat protein regulates transcription elongation through binding to the viral TAR RNA stem-loop structure. We have...
...; CH; RNA, Viral--metabolism--ME; Receptors, Cell Surface--genetics --GE; Recombinant Proteins--genetics--GE; Ribonucleases; Substrate Specificity; Transcription, Genetic--physiology--PH

5/6,K/4
DIALOG(R)File 155:
09572486 97456508 PMID: 9311822
A human primary T-lymphocyte-derived human immunodeficiency virus type 1 Tat-associated kinase phosphorylates the C-terminal domain of RNA polymerase II and induces CAK activity.
Oct 1997
Tat protein mediates transactivation of human immunodeficiency virus type 1 (HIV-1), which results in more-efficient...
...; metabolism--ME; Protein-Serine-Threonine Kinases --isolation and purification--IP; RNA Polymerase II--chemistry--CH; Substrate Specificity ; T-Lymphocytes--enzymology--EN; T-Lymphocytes--immunology--IM

5/6,K/5
DIALOG(R)File 155:
09563800 97471748 PMID: 9330689
CD26/dipeptidyl peptidase IV in lymphocyte growth regulation.
1997
... role of TGF-beta 1 in mediating CD26 function. X-X-Pro peptides as HIV- Tat protein strongly inhibit DP IV enzymatic activity and suppress DNA synthesis. This group of peptides may...
... regulatory function in lymphocytes. Further work is required to determine the natural ligands, i.e. substrates and effectors, which are play the central role in DP IV/CD26 action in T...

5/6,K/6
DIALOG(R)File 155:
09329614 97236791 PMID: 9079663
The Tat protein of human immunodeficiency virus type 1 is a substrate and inhibitor of the interferon-induced, virally activated protein kinase, PKR.
Mar 28 1997
... RNA-binding region of Tat. Tat competes with eukaryotic initiation factor 2, a well-characterized substrate of PKR, for phosphorylation by activated PKR. Tat also inhibits the autophosphorylation of PKR by...

5/6,K/7
DIALOG(R)File 155:
09111123 97005306 PMID: 8852605
CD26 mediates the action of HIV-1 Tat protein on DNA synthesis and cytokine production in U937 cells.
Jan 1996
The human immunodeficiency virus 1 (HIV-1) Tat protein is known to be capable of suppressing antigen- and CD3-induced activation of human T...
...to the dipeptidyl peptidase IV (DP IV, CD26) and inhibit the degradation of the chromogenic substrate Gly-Pro-p-nitroanilide. Using the method of free zone capillary electrophoresis, here we have...
...1 beta(1-6), and IL-6(1-12) was also significantly inhibited by the Tat protein . Moreover, HIV-1 Tat at a concentration of 10 micrograms/ml was found to have...
... IV/CD26 inhibitors (Immunobiol., 1994, vol. 192, pp. 121-136). These

data strongly suggest that Tat protein is a potent "natural" inhibitor of DP IV/CD26, and they support the hypothesis that...

5/6,K/8
DIALOG(R)File 155:
08915177 96256690 PMID: 8786430
Extracellular human immunodeficiency virus type 1 Tat protein promotes aggregation and adhesion of cerebellar neurons.
Apr 15 1996
Recombinant human immunodeficiency virus (HIV-1) Tat protein added to the culture medium of rat cerebellar neurons promoted aggregation and formation of spoke...
... deletion of the cysteine-rich domain had no effect on neuronal morphology. In contrast, a Tat protein that contained a deletion of the proline-rich domain promoted neuronal aggregation. Aggregation of neurons...
... domains of Tat required to induce aggregation also mediated adhesion of neurons to Tat-coated substrates . The HIV-2 Tat protein , which lacks an RGD sequence but contains cysteine-rich and basic domains similar to HIV-1 Tat, induced aggregation and acted as a substrate for adhesion when added at higher concentrations than HIV-1 Tat. Vitronectin, fibronectin, and RGD-containing peptides did not induce morphological changes in neurons or act as substrates for adhesion. The ability of Tat to induce morphological changes and promote adhesion was independent of the ability of Tat to transactivate HIV gene expression. Our results suggest that extracellular Tat protein most likely alters neuronal morphology and mediates adhesion by acting in a manner similar to...

5/6,K/9
DIALOG(R)File 155:
08904950 96256770 PMID: 8676484
The human immunodeficiency virus Tat proteins specifically associate with TAK in vivo and require the carboxyl-terminal domain of RNA polymerase II for function.
Jul 1996
... domain (CTD) of RNA polymerase II (RNAP II). We now show that the 42-kDa substrate of TAK cochromatographs with TAK activity, suggesting that this 42-kDa polypeptide is a subunit...
Chemical Name: Gene Products, tat ; Protein -Serine-Threonine Kinases; RNA Polymerase II

5/6,K/10
DIALOG(R)File 155:
08881669 96226178 PMID: 8657573
Fusion with an RNA binding domain to confer target RNA specificity to an RNase: design and engineering of Tat-RNase H that specifically recognizes and cleaves HIV-1 RNA in vitro.
May 15 1996
... human immunodeficiency virus type-1 (HIV-1) RNA as a model. Trans-activator of transcription (Tat) protein is one of the key regulatory proteins encoded by HIV-1. It binds to the...
...; Proteins--metabolism--ME; Ribonuclease H, Calf Thymus--chemistry--CH ; Ribonuclease H, Calf Thymus--metabolism--ME; Substrate Specificity; Trans-Activation (Genetics)

5/6,K/11
DIALOG(R)File 155:

08761286 96104282 PMID: 8574390
Inhibition of dipeptidyl peptidase IV (DP IV) by anti-DP IV antibodies and non- substrate X-X-Pro- oligopeptides ascertained by capillary electrophoresis.
Nov 17 1995
... zone capillary electrophoresis as an alternative peptidase assay. In contrast to the conventional DP IV substrate glycyl-prolyl-p-nitroanilide (Gly-Pro-pNA), the hydrolysis of this peptide by DP IV...
...DP IV antibodies. Inhibition of DP IV was also observed with a number of non- substrate oligopeptides containing an N-terminal X-X-Pro- structure, including the HIV Tat protein . For Met-IL-2(1-6), we determined a competitive inhibition with an inhibition constant...

5/6,K/12
DIALOG(R)File 155:
08728941 96074517 PMID: 7491766
HIV-1 Tat directly interacts with the interferon-induced, double-stranded RNA-dependent kinase, PKR.
Nov 10 1995
We present evidence that the HIV-1 Tat protein and the RNA-dependent cellular protein kinase, PKR, interact with each other both in vitro...
... vivo. Using GST fusion chromatography, we demonstrate that PKR, interacts directly with the HIV-1 Tat protein . The region in Tat sufficient for binding PKR maps within amino acids 20 to 72...
... by PKR, while the one exon form of Tat (Tat 72) inhibited PKR autophosphorylation and substrate phosphorylation. The ability of Tat to interact with PKR was demonstrated in both yeast and...

5/6,K/13
DIALOG(R)File 155:
08636368 95395931 PMID: 7666503
Potent inhibition of human immunodeficiency virus type 1 (HIV-1) replication by inducible expression of HIV-1 PR multimers.
Oct 1995
...placed under control of the HIV-1 long terminal repeat, thus requiring the HIV-1 Tat protein for expression of PR. The activity of PR was assessed by cotransfection with a construct producing a Gag substrate . Expression of PR as an intramolecular multimer resulted in a large increase in PR activity...

5/6,K/14
DIALOG(R)File 155:
08623703 95381609 PMID: 7653094
Human parainfluenza virus type 3: analysis of the cytoplasmic tail and transmembrane anchor of the hemagglutinin-neuraminidase protein in promoting cell fusion.
May 1995
... the cell types, HeLa-tat, constitutively expressed the human immunodeficiency virus type I (HIV-1) tat protein from a Moloney murine leukemia virus long terminal repeat (LTR), while the second cell type...
... which was then measured by direct staining of cells or using cell lysates with appropriate substrates . Cell fusion was observed only when both the HPIV3 F and functional HN proteins were...

5/6,K/16
DIALOG(R)File 155:

08156774 94294425 PMID: 7912830
Human immunodeficiency virus 1 Tat binds to dipeptidyl aminopeptidase IV (CD26): a possible mechanism for Tat's immunosuppressive activity.
Jul 5 1994
The human immunodeficiency virus 1 (HIV-1) Tat protein suppresses antigen-induced, but not mitogen-induced, activation of human T cells when added to...
... at physiological salt concentrations without inhibiting the protease activity of DP IV against small chromogenic substrates used to assay activity, but Tat markedly inhibits the activity of DP IV at lower...

5/6,K/18
DIALOG(R)File 155:
07796926 93324319 PMID: 8332456
Design and synthesis of RNA miniduplexes via a synthetic linker approach. 2. Generation of covalently closed, double-stranded cyclic HIV-1 TAR RNA analogs with high Tat-binding affinity.
Jun 11 1993
...on the HIV-1 TAR RNA hairpin were shown to be thermodynamically stable and good substrates for binding by the HIV-1 Tat protein which normally bind to natural TAR (6). In this study, we have extended our studies...
... or synthetic linkers (derivatized from hexaethylene glycol), the resulting cyclic TAR RNA analogs were good substrates for binding by both Tat-derived peptide or full-length Tat protein . Interestingly, the cyclic TAR analogs failed to show any binding if the synthetic linker was...

5/6,K/19
DIALOG(R)File 155:
07671933 93195920 PMID: 8450529
Hydrogen-bonding contacts in the major groove are required for human immunodeficiency virus type-1 tat protein recognition of TAR RNA.
Mar 5 1993
... site for tat on TAR RNA was analysed by preparing a series of model RNA substrates carrying site-specific functional group modifications. The test RNAs were prepared by annealing two short...

5/6,K/20
DIALOG(R)File 155:
07516306 93041713 PMID: 1384694
RNA binding assays for Tat-derived peptides: implications for specificity.
Oct 27 1992
RNA recognition by the HIV Tat protein is mediated in part by an arginine- and lysine-rich basic subdomain implicated as a...
...; Competitive; Kinetics; Mathematics; Molecular Sequence Data; Nucleic Acid Conformation; Osmolar Concentration; RNA--chemical synthesis--CS; Substrate Specificity

5/6,K/21
DIALOG(R)File 155:
06052989 89125710 PMID: 2536828
Mutational analysis of the conserved basic domain of human immunodeficiency virus tat protein .
Mar 1989
... were found to impair both the in vivo stability and the nuclear localization of the tat protein . It is proposed that this protein

domain serves to efficiently target the tat gene product to its appropriate site or substrate within the nucleus of expressing cells.

5/7/15
DIALOG(R)File 155:MEDLINE(R)
08525926 95281551 PMID: 7539135
Angiogenic properties of human immunodeficiency virus type 1 Tat protein .
Albini A; Barillari G; Benelli R; Gallo R C; Ensoli B
Laboratory of Tumor Cell Biology, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) May 23 1995, 92 (11) p4838-42, ISSN 0027-8424 Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Extracellular human immunodeficiency virus type 1 (HIV-1) Tat protein promotes growth of spindle cells derived from AIDS-associated Kaposi sarcoma (AIDS-KS), an angioproliferative disease very frequent in HIV-1-infected individuals. Normal vascular cells, progenitors of AIDS-KS cells, proliferate in response to Tat after exposure to inflammatory cytokines, whose levels are augmented in HIV-1-infected individuals and in KS lesions. Here we show that Tat also promotes AIDS-KS and normal vascular cells to migrate and to degrade the basement membrane and stimulates endothelial cell morphogenesis on a matrix substrate . These effects are obtained at picomolar concentrations of exogenous Tat and are promoted by the treatment of the cells with the same inflammatory cytokines stimulating expression of the receptors for Tat, the integrins alpha 5 beta 1 and alpha v beta 3. Thus, under specific circumstances, Tat has angiogenic properties. As Tat and its receptors are present in AIDS-KS lesions, these data may explain some of the mechanisms by which Tat can induce angiogenesis and cooperate in the development of AIDS-KS.
Record Date Created: 19950629

5/7/17
DIALOG(R)File 155:MEDLINE(R)
07934382 94069933 PMID: 8249283
Specific interaction of the human immunodeficiency virus Tat proteins with a cellular protein kinase.
Herrmann C H; Rice A P
Baylor College of Medicine, Division of Molecular Virology, Houston, Texas 77030.
Virology (UNITED STATES) Dec 1993, 197 (2) p601-8, ISSN 0042-6822 Journal Code: 0110674
Contract/Grant No.: AI-25308; AI; NIAID
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2) Tat proteins are related transcriptional activators whose effects are likely to be mediated by a cellular factor. Using an in vitro kinase assay, we have shown that the Tat protein of HIV-2 and the activation domain of the Tat protein of HIV-1 specifically bind to a cellular protein kinase.

Mutations in Tat that abolish transactivation activity in vivo abrogate the ability of the mutants to bind to the kinase in vitro. This is the first demonstration of a cellular factor that binds to Tat that is specific for a functional activation domain of Tat and that displays a biochemical activity. Additionally, we show that the Tat protein of HIV-2 serves as a substrate of the kinase in vitro. Consistent with the in vitro results, the Tat protein of HIV-2 interacts with a cellular kinase in HIV-2 Tat-transfected cells and is phosphorylated in vivo. These results suggest that a cellular serine/threonine kinase may act as a mediator of Tat function.
Record Date Created: 19931223

16/6,K/1
DIALOG(R)File 155:
13375030 22048038 PMID: 12052871
Phosphorylation of the RNA polymerase II carboxyl-terminal domain by CDK9 is directly responsible for human immunodeficiency virus type 1 Tat-activated transcriptional elongation.
Jul 2002
Stimulation of transcriptional elongation by the human immunodeficiency virus type 1 Tat protein is mediated by CDK9, a kinase that phosphorylates the RNA polymerase II carboxyl-terminal domain...
...Under these chase conditions, efficient rephosphorylation of the CTD was observed in complexes containing the Tat protein but not in transcription complexes prepared in the absence of Tat protein . Immunoblots and kinase assays with synthetic peptides showed that Tat activated CDK9 directly since the enzyme and its cyclin partner, cyclin...
... is due to CTD phosphorylation alone, since even after the removal of Spt5, the second substrate for CDK9, RNA polymerase elongation is enhanced by Tat-activated CDK9 activity. We conclude that...

16/6,K/2
DIALOG(R)File 155:
12555115 21451167 PMID: 11567105
Heparin binding by the HIV-1 tat protein transduction domain.
Oct 2001
The protein transduction domain from the HIV-1 tat protein (termed PTD-tat) has been fused to the C-terminus of a model cargo protein...
; Heparitin Sulfate--metabolism--ME; Nerve Tissue Proteins--metabolism --ME; Protein Structure, Tertiary--physiology--PH; Protein Transport; Streptococcus--chemistry--CH
Chemical Name: G- substrate ; Gene Products, tat; Nerve Tissue Proteins ; Heparin; Heparitin Sulfate

16/6,K/3
DIALOG(R)File 155:
10169856 99138948 PMID: 9973525
Extracellular HIV-1 tat protein up-regulates the expression of surface CXC-chemokine receptor 4 in resting CD4+ T cells.
Feb 15 1999
Here we report that synthetic HIV-1 Tat protein , immobilized on a solid substrate , up-regulates the surface expression of the CXC-chemokine receptor 4 (CXCR4), but not of...
...by the protein synthesis inhibitor cycloheximide, clearly indicating the requirement of de novo synthesis. As Tat protein is actively released by HIV-1 infected cells, our data indicate a potentially important role...

Chemical Name: Gene Products, tat ; Proteins ; Receptors, CXCR4

16/6,K/4
DIALOG(R)File 155:
09111123 97005306 PMID: 8852605
CD26 mediates the action of HIV-1 Tat protein on DNA synthesis and cytokine production in U937 cells.
Jan 1996
The human immunodeficiency virus 1 (HIV-1) Tat protein is known to be capable of suppressing antigen- and CD3-induced activation of human T...
...to the dipeptidyl peptidase IV (DP IV, CD26) and inhibit the degradation of the chromogenic substrate Gly-Pro-p-nitroanilide. Using the method of free zone capillary electrophoresis, here we have...
...1 beta(1-6), and IL-6(1-12) was also significantly inhibited by the Tat protein . Moreover, HIV-1 Tat at a concentration of 10 micrograms/ml was found to have...
...cytokine production of low CD26-expressing U937-L cells. Similar results have been found with synthetic DP IV/CD26 inhibitors (Immunobiol., 1994, vol. 192, pp. 121-136). These data strongly suggest that Tat protein is a potent "natural" inhibitor of DP IV/CD26, and they support the hypothesis that...

16/6,K/5
DIALOG(R)File 155:
07796926 93324319 PMID: 8332456
Design and synthesis of RNA miniduplexes via a synthetic linker approach. 2. Generation of covalently closed, double-stranded cyclic HIV-1 TAR RNA analogs with high Tat-binding affinity.
Jun 11 1993
... double-stranded oligonucleotides whereby one end of the duplex was joined and stabilized by a synthetic linker of specific design (miniduplexes)(6). Model miniduplexes based on the HIV-1 TAR RNA hairpin were shown to be thermodynamically stable and good substrates for binding by the HIV-1 Tat protein which normally bind to natural TAR (6). In this study, we have extended our studies...
... RNA stem (9 bp) were covalently linked through either nucleotidic loops (4-6 nt) or synthetic linkers (derivatized from hexaethylene glycol), the resulting cyclic TAR RNA analogs were good substrates for binding by both Tat-derived peptide or full-length Tat protein . Interestingly, the cyclic TAR analogs failed to show any binding if the synthetic linker was reduced in length (e.g. derivatized from triethylene glycol), although such linkers are...

16/6,K/6
DIALOG(R)File 155:
07671933 93195920 PMID: 8450529
Hydrogen-bonding contacts in the major groove are required for human immunodeficiency virus type-1 tat protein recognition of TAR RNA.
Mar 5 1993
... site for tat on TAR RNA was analysed by preparing a series of model RNA substrates carrying site-specific functional group modifications. The test RNAs were prepared by annealing two short synthetic oligoribonucleotides to form a duplex structure with a U-rich bulge and flanking sequences identical...

File 155:MEDLINE(R) 1966-2002/Sep W5

Set	Items	Description
S1	876	TAT()PROTEIN
S2	182342	SUBSTRATE?
S3	37	S1 AND S2
S4	16	S3/2002 OR S3/2001 OR S3/2000 OR S3/1999
S5	**21**	**S3 NOT S4**
S6	0	POLYPEPTIDE()GROWTH()FACTOR? ? AND TAT()PROTEIN? ? AND (VEGF OR VASCULAR()ENDOTHELIAL()GROWTH()FACTOR? ?)
S7	919	TAT()PROTEIN? ?
S8	182331	SUBSTRATE? ?
S9	17901	BIOCOMPATIBLE
S10	302	BIORESORBABLE
S11	238476	ARTIFICIAL OR SYNTHETIC
S12	812627	TISSUE OR ORGAN
S13	225247	PROSTHES?S OR GRAFT? ?
S14	41	S7 AND S8
S15	1206826	S11:S13
S16	**6**	**S14 AND S9:S13**

L15 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:391625 HCAPLUS
DN 136:391075
TI Electroprocessed collagen as extracellular matrix for implants

L15 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:487235 HCAPLUS
DOCUMENT NUMBER: 131:120914
TITLE: **Prostheses with associated growth factors**
INVENTOR(S): Carlyle, Wenda C.; Kelly, Sheila J.; Ogle, Matthew F.
PATENT ASSIGNEE(S): St. Jude Medical, Inc., USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937337	A2	19990729	WO 1999-US1391	19990121
WO 9937337	A3	19990930		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2319000	AA	19990729	CA 1999-2319000	19990121
AU 9924658	A1	19990809	AU 1999-24658	19990121
EP 1051204	A2	20001115	EP 1999-904210	19990121
R: CH, DE, ES, FR, GB, IT, LI, NL, IE				
BR 9907273	A	20010904	BR 1999-7273	19990121
JP 2002500929	T2	20020115	JP 2000-528316	19990121

PRIORITY APPLN. INFO.: US 1998-14087 A 19980127

US 1998-186810 A 19981105
WO 1999-US1391 W 19990121

AB A polypeptide growth factor is assocd. with a ***substrate*** to promote population of the ***substrate*** with endothelial cells. A **prosthesis is formed with growth factor ***crosslinked*** to the ***substrate*** .** Preferred polypeptide growth factors include VEGF. VEGF treated tissue can be populated with endothelial cells in vitro and/or in vivo. In an alternative approach, VEGF can be assocd. with the ***substrate*** by direct contact with a VEGF soln., application of the VEGF with an adhesive as a coating to the ***substrate*** , or chem. binding of the VEGF to the ***substrate*** with or without an intervening linker mol. In one preferred approach, the growth factor is assocd. with the ***substrate*** by ***crosslinking*** under suitably mild conditions such that the growth factor is active following the ***crosslinking*** process.

L17 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2002 ACS
AN 2002:522546 HCAPLUS
DN 137:83728
TI Electroprocessed collagen for extracellular matrix

L17 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:728863 HCAPLUS
DN 136:83255
TI Fibroblasts in mechanically stressed collagen lattices assume a " ***synthetic*** " phenotype

L17 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:593777 HCAPLUS
DN 134:110176
TI Hammerhead ribozyme specifically inhibits vascular endothelial growth factor gene expression in a human hepatocellular carcinoma cell line

L17 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:706427 HCAPLUS
DN 130:77785
TI Characterization and Kinetic Mechanism of Catalytic Domain of Human Vascular Endothelial Growth Factor Receptor-2 Tyrosine Kinase (VEGFR2 TK), a Key Enzyme in Angiogenesis

L17 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:592758 HCAPLUS
DN 129:298672
TI Protein kinase G mediates vascular endothelial growth factor-induced Raf-1 activation and proliferation in human endothelial cells

L17 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:441541 BIOSIS
TI Inhibition of angiogenesis by the cancer chemopreventive agent conjugated linoleic acid.

L17 ANSWER 9 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2002272980 EMBASE
TI Inhibition of angiogenesis by the cancer chemopreventive agent conjugated linoleic acid.

L17 ANSWER 10 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2001205323 EMBASE
TI Covalently conjugated VEGF-fibrin matrices for endothelialization.

L17 ANSWER 11 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 1998307116 EMBASE
TI Protein kinase G mediates vascular endothelial growth factor-induced Raf-1 activation and proliferation in human endothelial cells.

L17 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:816702 HCAPLUS
DOCUMENT NUMBER: 135:376688
TITLE: Growth factor modified protein matrices for tissue engineering
INVENTOR(S): Hubbell, Jeffrey A.; Schense, Jason C.; Sakiyama-elbert, Shelly E.
PATENT ASSIGNEE(S): Eidgenossisch Technische Hochschule Zurich, Switz.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083522	A2	20011108	WO 2000-US11947	20000501
WO 2001083522	A3	20020328		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AB Proteins are incorporated into protein or polysaccharide matrixes for use in tissue repair, regeneration and/or remodeling and/or drug delivery. The proteins can be incorporated so that they are released by degrdn. of the matrix, by enzymic action and/or diffusion. As demonstrated by the examples, one method is to bind heparin to the matrix by either covalent or non-covalent methods, to form a heparin-matrix. The heparin then non-covalently binds heparin-binding growth factors to the protein matrix. Alternatively, **a fusion protein can be constructed which contains a ***crosslinking*** region such as a factor XIIIa ***substrate*** and the native protein sequence.** Incorporation of degradable linkages between the matrix and the bioactive factors can be particularly useful when long-term drug delivery is desired, for example in the case of nerve regeneration, where it is desirable to vary the rate of drug release spatially as a function of regeneration, e.g. rapidly near the living tissue interface and more slowly farther into the injury zone. Addnl. benefits include the lower total drug dose within the delivery system, and spatial regulation of release which permits a greater percentage of the drug to be released at the time of greatest cellular activity.

L17 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:405706 HCAPLUS
DOCUMENT NUMBER: 135:362486
TITLE: Covalently conjugated VEGF-fibrin matrixes for endothelialization
AUTHOR(S): Zisch, A. H.; Schenk, U.; Schense, J. C.; Sakiyama-Elbert, S. E.; Hubbell, J. A.
CORPORATE SOURCE: Department of Materials and Institute for Biomedical Engineering, ETH and University of Zurich, Zurich, 8044, Switz.
SOURCE: Journal of Controlled Release (2001), 72(1-3), 101-113
CODEN: JCREEC; ISSN: 0168-3659
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Vascular endothelial growth factor (VEGF) is a key factor in endothelial cell biol. and blood vessel formation and a candidate therapeutic for the stimulation of angiogenesis-dependent tissue regeneration. The objective of this study was to confer the angiogenic activity of VEGF121 upon the biomaterial fibrin, a natural ***substrate*** for endothelial cell growth and clin. accepted as 'fibrin glue'. To achieve this, the authors engineered fibrin-based hydrogels that were covalently modified with VEGF121. Our lab. has recently developed novel methodol. that allows the covalent incorporation of exogenous bioactive peptides by the transglutaminase activity of factor XIIIa into fibrin during coagulation. Here, this ability of factor XIIIa to ***crosslink*** addnl. proteins within fibrin was employed to covalently incorporate VEGF121. By recombinant DNA methodol., a mutant VEGF121 variant, .alpha.2-PI1-8-VEGF121, which contains an addnl. factor XIIIa ***substrate*** sequence NQEQVSPL at the aminoterminus, was expressed in E. coli. In sol. form, the mutant protein fully retained its mitogenic activity for endothelial cells. Using 125I-labeled .alpha.2-PI1-8-VEGF121, its covalent incorporation and the efficiency of incorporation into fibrin was demonstrated and characterized. The immobilized, fibrin-conjugated VEGF121 protein remained an active and very efficient mitogen for human endothelial cells grown on two-dimensional VEGF121-modified fibrin surfaces, and the incorporation of increasing amts. of .alpha.2-PI1-8-VEGF121 resulted in dose-dependent enhancement of endothelial cell growth. The VEGF-modified fibrin matrixes can be formed as injectable gels in a single-step reaction under physiol. conditions in vivo. When used as a ingrowth matrix, such VEGF incorporating materials could be useful in a variety of clin. situations that require an angiogenic response into an ischemic region or implant.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'HOME' ENTERED AT 14:36:14 ON 10 OCT 2002)
FILE 'REGISTRY' ENTERED AT 14:36:22 ON 10 OCT 2002
E TAT PROTEIN/CN
L1 7 S E4-E10
E TAT PROTEIN (BOVINE/CN
E TAT PROTEIN (HUMAN/CN
L2 9 S E4-E12
L3 212 S TAT PROTEIN?/CN
E POLYPEPTIDE GROWTH FACTOR/CN
E VEGF/CN

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L4            51 S VEGF?/CN
                 E VASCULAR ENDOTHELIAL GROWTH FACTOR/CN
L5             1 S E3
     FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 14:41:16 ON
     10 OCT 2002
L6         18614 S L3 OR L4 OR L5
L7       1283827 S SUBSTRATE
L8       1467672 S ARTIFICIAL OR SYNTHETIC
L9           267 S BIOCOMPATIBLE AND BIORESORBABLE
L10       271293 S CROSSLINK?
L11          112 S L6 AND L7
L12            5 S L10 AND L11
L13           10 S L11 AND L8
L14            0 S L11 AND L9
L15            2 S L12 AND L13
L16           13 S L12 OR L13
L17           11 S L16 NOT L15
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